TasP

Antiretroviral Treatment as Prevention • ANRS 12249

Ukuphila kwami, ukuphila kwethu (my health for our health)

ADDRESSING SOCIAL SCIENCE IN A HIV TREATMENT AS PREVENTION TRIAL IN SOUTH AFRICA

Joseph Larmarange, John Imrie,
Joanna Orne-Gliemann, Collins Iwuji, France Lert
for the ANRS 12249 TasP Study Group

ASSHH Conference, Paris, July 2013

CONTEXT

Using ARVs for prevention

- Since 1994, this concept has expanded
  - Successfully implemented for Mother to Child transmission
  - Used for post-exposure prophylaxis
  - Ongoing research on:
    - Microbicides with ARVs
    - Pre-exposure prophylaxis

- ARVs control HIV viral load &
  Viral load is the dominant determinant of sexual transmission (Quinn et al. 2000 NEJM; Garcia et al. 1999 NEJM)

2008: the Swiss Statement

HIV-infected individuals on ART with undetectable viral load for 12 months and no other IST don't transmit HIV sexually anymore and could stop using a condom within a stable couple

CFS

AUTRES GROUPEMENTS ET INSTITUTIONS

Les personnes séropositives ne souffrant d'aucune autre MST et suivant un traitement antirétroviral efficace ne transmettent pas le VIH par voie sexuelle

Could ARV treatment contribute to reduce HIV transmission at individual and population levels?

2009: the "Granich model"

Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model

Reuben M Granich, Charles F Gilks, Christopher Dye, Kevin M De Cock, Brian G Williams

Lancet 2009; 373: 48–57

Published Online November 26, 2008 DOI:10.1016/S0140-6736(08)61697-9

See Comment pages 7 and 9

Department of HIV/AIDS (R M Granich MD, Prof C F Gilks DPhil, Prof K M De Cock MD) **and Stop TB Department** (Prof C Dye DPhil, B G Williams PhD), **WHO, Geneva, Switzerland**

Summary

Background Roughly 3 million people worldwide were receiving antiretroviral therapy (ART) at the end of 2007, but an estimated 6·7 million were still in need of treatment and a further 2·7 million became infected with HIV in 2007. Prevention efforts might reduce HIV incidence but are unlikely to eliminate this disease. We investigated a theoretical strategy of universal voluntary HIV testing and immediate treatment with ART, and examined the conditions under which the HIV epidemic could be driven towards elimination.

Methods We used mathematical models to explore the effect on the case reproduction number (stochastic model) and long-term dynamics of the HIV epidemic (deterministic transmission model) of testing all people in our test-case community (aged 15 years and older) for HIV every year and starting people on ART immediately after they are diagnosed HIV positive. We used data from South Africa as the test case for a generalised epidemic, and assumed that all HIV transmission was heterosexual.

Universal testing with immediate antiretroviral therapy could eliminate HIV transmission

(model calculated in the context of South Africa)

2011: HPTN 052 study

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 11, 2011 VOL. 365 NO. 6

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D., Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D., Sanjay Mehendale, M.D., Suwat Chariyalertsak, M.D., Breno R. Santos, M.D., Kenneth H. Mayer, M.D., Irving F. Hoffman, P.A., Susan H. Eshleman, M.D., Estelle Piwowar-Manning, M.T., Lei Wang, Ph.D., Joseph Makhema, F.R.C.P., Lisa A. Mills, M.D., Guy de Bruyn, M.B., B.Ch., Ian Sanne, M.B., B.Ch.,

The early initiation of antiretroviral therapy reduces rates of sexual transmission of HIV-1 by 96%

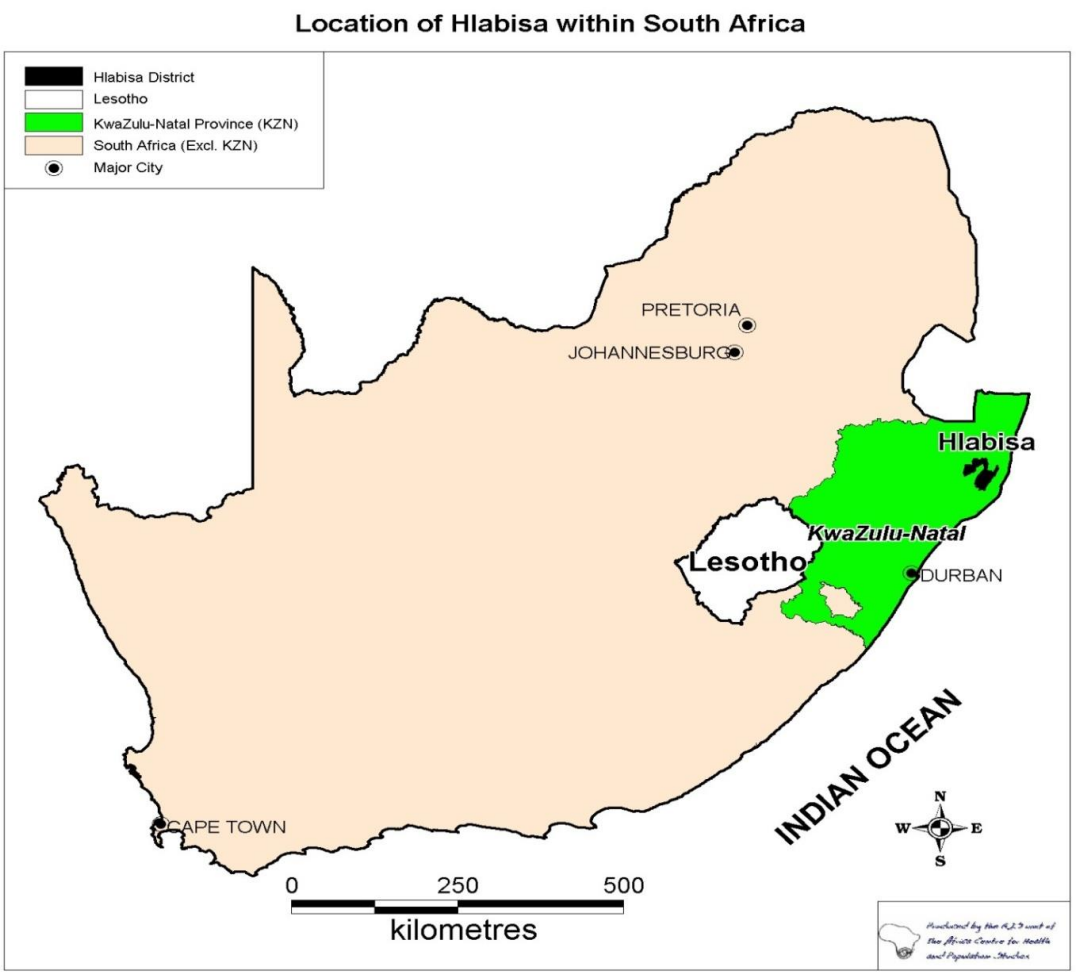
The TasP ANRS 12249 project

Antiretroviral Treatment as Prevention of HIV

Main hypothesis

HIV testing of all adult members of a community,
followed by immediate ART initiation
of all, or nearly all, HIV-infected participants
regardless of immunological or clinical staging
will prevent onward transmission
and reduce HIV incidence in this population

Hlabisa sub-district (South Africa)



- Rural area of 1430 km²
- Approx. 220 000 inhabitants speaking isiZulu
- HIV prevalence: 24% among adults

TasP trial design

- TasP is a cluster randomized trial.
  - Each cluster has a population of approx. 1250 adults (16+ years).
  - The **TasP intervention** has 2 components:
    "universal" repeat testing (all clusters) + early treatment (intervention cluster)

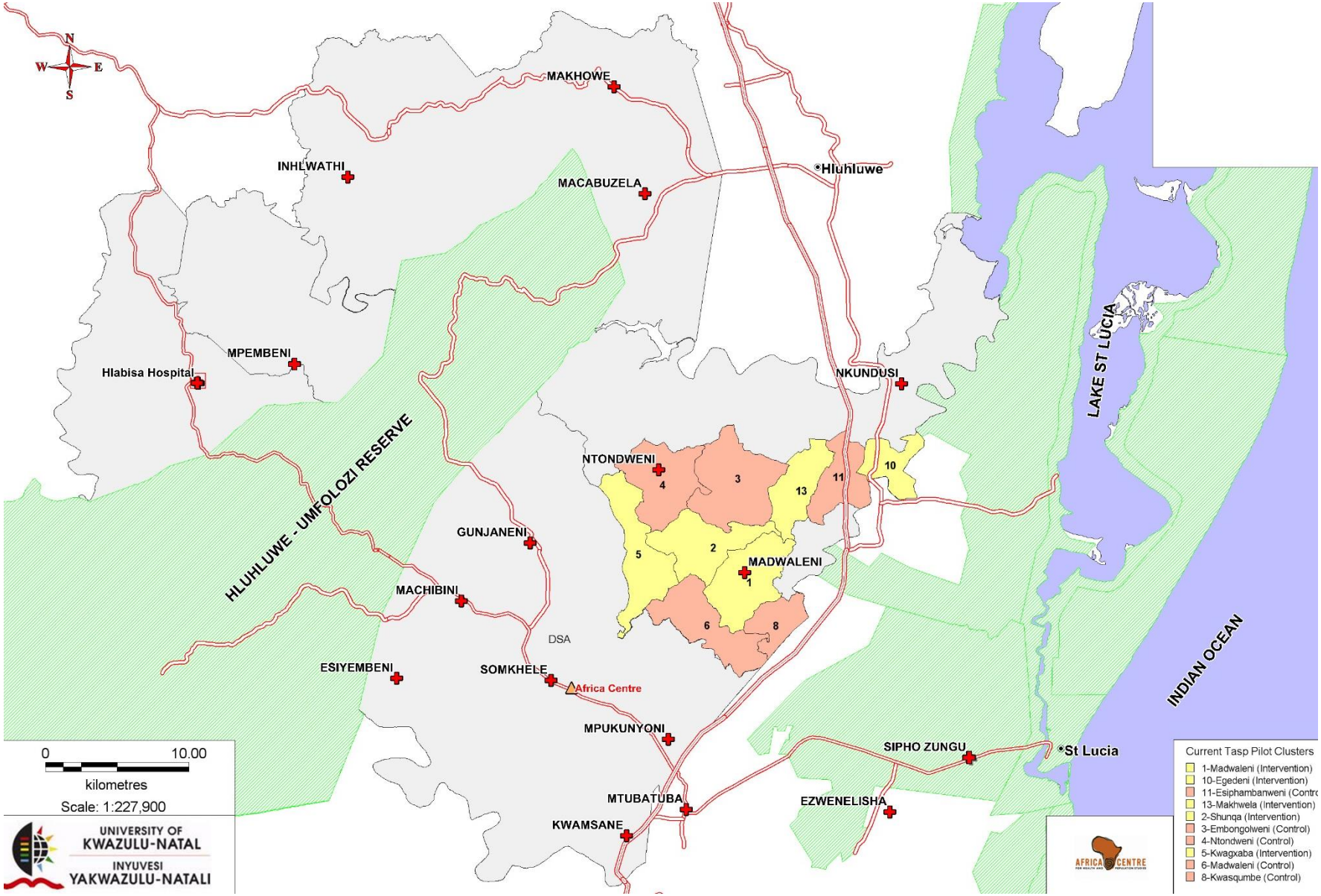
- In each cluster, rounds of **home-based HIV testing** repeated every 4 to 6 months
- All HIV+ identified participants are referred to local TasP clinics (at least one fixed or mobile clinic per cluster)

Control clusters	Intervention clusters
ARV treatment according to national guidelines (<350 CD4 or WHO stage 3 or 4)	ARV treatment regardless of CD4 or clinical staging

Implementation in 2 phases

- Phase 1
  - Objective: to assess **acceptability** of the TasP intervention (repeat testing + early treatment) and **feasibility** of the trial (in particular regarding statistical power)
  - Implemented in
    4 clusters since March 2012
    + 6 clusters since January 2013
  - Analysis of phase 1 planned in 2014
- Phase 2
  - Will depend of results of phase 1

Hlabisa sub-district with phase 1 clusters



Social science research questions

Social science research questions

- TasP is not just a biomedical intervention but raises also unprecedented social challenges
  - To be successful, the TasP intervention requires changes of social representations and individual perceptions and behaviours

- Social science questions addressed in the ANRS 12249 TasP project could be classified in 2 main areas
  - Comprehensive understanding of barriers at each step of the TasP "cascade" (uptake of testing and care)
  - Social and economic consequences of the TasP intervention at individual (both HIV- and HIV+), family and community levels

Uptake of testing and care

- Some aspects already well documented in different settings, but not in a such context of intensification of providing the interventions (testing and treatment)

- Example: the Granich model assumed that 90% of people are tested and 90% of HIV+ are on ARV treatment
  - Much higher that was observed so far
  - Uptake of home-based HIV testing
    58 to 92% in 5 different studies in South Africa
    (Sabapathy et al. 2012)
  - Linkage to care & starting treatment
    for 100 patients in Africa with a HIV+ test, 72 had a CD4 count, 40 were eligible and 25 started ARVs (Mugglin et al. 2012)

New issues

- According to the Granich model, elimination of the epidemic may be envisaged only if
  - HIV- are tested at least every year
  - HIV+ start ARVs with >800 CD4

- **Repeat testing** has been rarely documented
  - In published papers, repeat test was proposed after 2 or more years
  - How acceptable will be routine repeated HIV testing?

- **Early treatment**
  - Could the availability of ARVs regardless of CD4 count have an impact (or not) on linkage to care?
  - Acceptability of starting a treatment when you still feel healthy?
  - What will be adherence and retention among HIV+ starting a treatment at high CD4 count?

Potential counterbalancing effects

- Will the overall effect of ART on HIV incidence be sufficiently important not to be counterbalanced at population levels by other potential effects?
  - ↗ ART coverage ➡ ↘ mortality ➡ ↗ HIV prevalence (Zaidi et al 2013)
  - ↗ ART coverage ➡ ↗ health (HIV+) ➡ ↗ sexual activity (HIV+) ?
    - Recent work at AC found no difference in sexual activity between those on ART and those not yet on ART (with CD4 > 500)
  - Knowledge of TasP effect ➡ ↘ condom use ?
    - Recent results from Temprano Social (Ivory Coast) suggest that condom use is the same among HIV+ with early vs. delayed treatment.
    - What about sexual and preventive behaviours in general population among HIV-?

Impact of TasP intervention

- How TasP will **impact on HIV infected people's life** in terms of of quality of life; HIV disclosure; stigmatization, relationships; sexual behaviors; perceptions; social support; treatment experience and adherence?
  - Example: could universal testing of all a community induce a sort of "obliged" HIV status disclosure to partners, family and other community members? How to keep secret your infection in a context where everyone would have been tested?
- What are the **changes at community level** during TasP implementation and influences on individual behaviors?
  - Example: will such a "massive" intervention increase stigma and marginalization of HIV+, or rather the opposite, contribute to a normalization of HIV and a better acceptability of people living with HIV?
  - Changes of social representations of HIV, transmission, treatment, prevention, testing in the general population?

Economic impact

- **Economic impact on the household** welfare (health care use and health care expenditures)
  - Being on care induces extra-expanses such as transportation cost, food, children supervision, work days lost, etc.
  - Budget impact

- If effective, the **cost-effectiveness** of the TasP intervention needs to be demonstrated in the context of scarce resources

Implementation

Quantitative and qualitative research tools are implemented at each stage of the TasP intervention to address the research questions

Tools implemented

- **Among all participants**
  - The **home-based questionnaires (repeated every 6 months)** document
    - knowledge/beliefs about HIV infection,
    - knowledge/expectations about treatment,
    - lifetime HIV testing history,
    - HIV testing attitudes/beliefs,
    - community stigma,
    - health care use and expenditure.
    - sexual partnerships,
    - condom use,
    - circumcision status,
    - risk behaviors,
    - quality of life,
  - **Focus groups and in-depth interviews** focus on mapping health services on the community, community understanding of HIV and the TasP intervention, local culture to support regular and repeated HIV testing

Tools implemented

- Among all participants

- **Among HIV infected participants**
  - **Questionnaires conducted in TasP clinics** both by ART counsellors and independent interviewers provide information regarding
    - ART perception and decision,
    - disclosure,
    - relationships,
    - satisfaction with care,
    - economic situation.
    - social and community support,
    - ART knowledge, adherence,
    - quality of life,
    - perceived stigma,
  - A **socio-psychological sub-study** among HIV-infected participants diagnosed HIV-positive but **not seen in clinics** will explore obstacles and barriers of linkage and entry into care

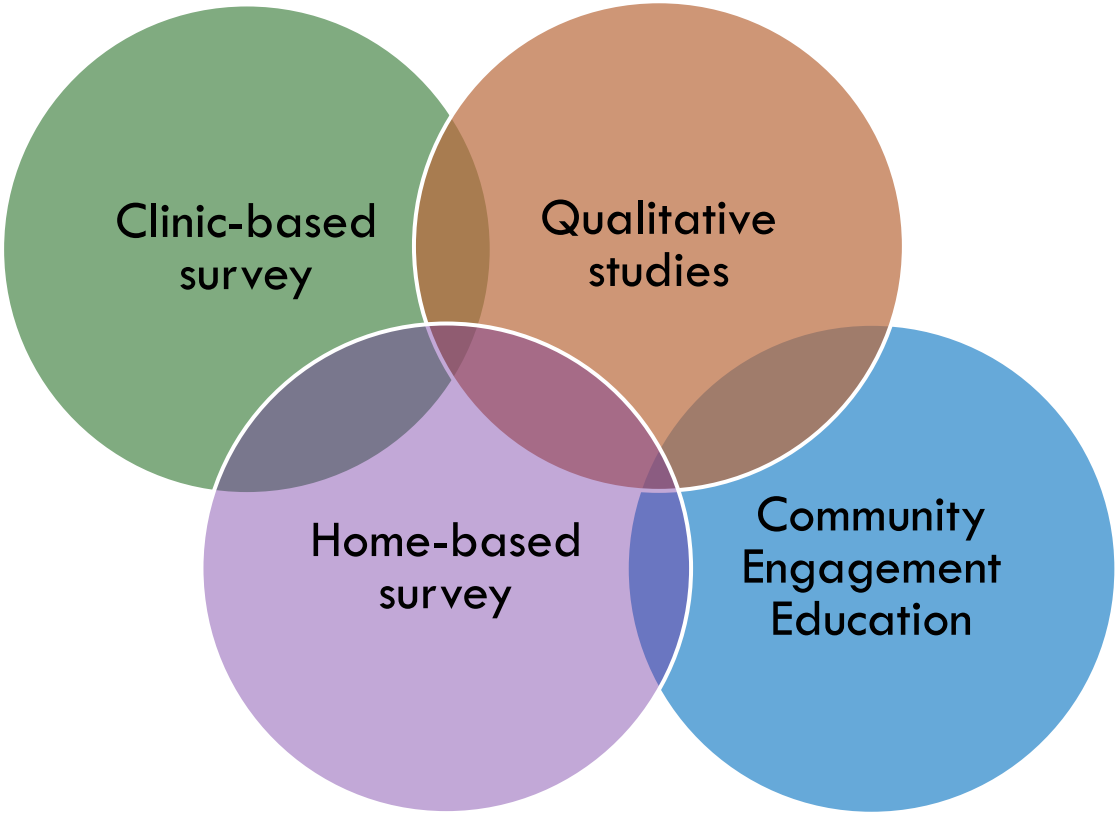
Tools implemented

- Among all participants
- Among HIV infected participants

- **Community engagement**
  - **Community engagement meetings** and **road shows** are organized in each cluster. They facilitate education about what TasP means and involves and allows additional clarification of what project implementation involves

Conclusion

Discussion



Triangulation of Social Science Studies will provide comprehensive insights, complementary to clinical and epidemiological outcomes, on the acceptability and effectiveness of TasP at individual, community, patient and health system level

Discussion

- Analyses of phase 1 planned for 201
- Only short and mid term (2-4 years) changes will be investigated in the trial
- Social science components in TasP trials will not be enough to answer emerging public health and operational questions relating to operational scale-up of "test and treat" interventions
  - See "Issues Emerging From Universal Test And Treat (UTT) Intervention Trials" presentation at 14h30 Room 3

TasP Study Group

Marie-Louise Newell (Co-PI, Africa Centre)
Francois Dabis (Co-PI, Inserm ISPED)
Collins Iwuji (Trial Coordinator/Physician, AC)
Joanna Orne-Gliemann (Trial Coordinator, ISPED)
Nonhlanhla Okesola (Africa Centre)
John Imrie (Africa Centre)
Till Barnighausen (Africa Centre)
Ruth Bland (Africa Centre)
Richard Lessells (Africa Centre)
Frank Tanser (Africa Centre)
Tulio de Oliviera (Africa Centre)
Johannes Viljoen (Africa Centre)
Colin Newell (Africa Centre)
Kevi Naidu (Africa Centre)
France Lert (Inserm CESP)
Rosemary Dray-Spira (Inserm CESP)
Joseph Larmarange (IRD CEPED, Africa Centre)
Bruno Spire (Inserm SE4S)
Sylvie Boyer (Inserm SE4S)
Alexandra Calmy (HUG Genève)
Marie-Laure Chaix (Université Paris Descartes)
Sophie Karcher (Inserm ISPED)
Rodolphe Thiebaut (Inserm ISPED)
Ken Freedberg (Massachussets General Hospital)

Acknowledgements

The French National Agency for Aids and Viral Hepatitis Research (ANRS) is the sponsor of the TasP trial.

The ANRS and the Deutsche Gesellschaft fur Internationale Zusammenarbeit (GIZ) GmbH provided funding for first phase of the trial.

The trial is conducted with the support of MERCK & Co. Inc and Gilead Sciences that provided Atripla® drug supply.

The Africa Centre receives core funding from the Wellcome Trust, which provides the basis for the population- and clinic-based research at the Centre.